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The flexibility of the complexed ligand causes ^{13}C relaxation times of all periphery carbons to drop without significant selectivity. Rotational energy barrier measurements of the methyl groups of the complexed ligand also show that the (*S,S*)-host-(*R*)-guest is the more stable complex.

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The Structures of the Chiral Dimethylpyridino-18-crown-6-α-(1-naphthyl)ethylammonium Perchlorate Complex as Determined by T1 Relaxation and Molecular Modeling

by

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Enantiomeric recognition of chiral organic ammonium salts by many chiral pyridino-crown macrocyclic ligands has been studied by NMR spectroscopy, calorimetric titration, solvent extraction, liquid membrane transport and chromotography. However, the interactions of most of the reported chiral ligands with enantiomeric guests have not been well characterized from either a thermodynamic or a kinetic standpoint.[1] Structural and conformational studies of complexes in solution could provide evidence for the basis of enantiomeric recognition. The primary binding force between the ligand and the primary ammonium cation is that formed by the three hydrogen bonds as shown in Figure 1.[2,3] The effects of tripod hydrogen bonding on ^{13}C relaxation times in the complex are reported here.

Experimental

^{13}C T1 Measurements: All glassware was washed with a 0.1 M EDTA solution to remove all possible paramagnetic impurities. The sample solutions were prepared as described above for the NOESY experiments to give a concentration of 0.20 M. Relaxation time measurements were performed at 125.67 MHz under proton-noise decoupling conditions by the inversion-recovery technique. Recovery delays were 30 seconds or longer. At least nine points were included for each T1 calculation. Usually, 150-200 scans were necessary for each recovery value in order to obtain an acceptable signal-to-noise ratio. All spectra were recorded at 25 °C. The calculation of T1 values was performed using software supplied by the spectrometer manufacturer using direct least squares fitting to a multiparameter exponential equation. At least two runs were

made for each system. The standard error was approximately 5% based on the values from all runs.

Molecular Mechanics Calculations: The conformational searches and comparisons of the lowest energy comformations of (*S*,*S*)-Me_2P18C6 complexes with (*R*) and (*S*)-NapEt were performed on a Silicon Graphics Personal IRIS workstation using QUANTA/CHARMm software from Molecular Simulations, Inc.

Results and Discussion

The tripod hydrogen bonding shown in Figure 1 could affect recognition in these systems. An attempt to determine the formation and location of these bonds was made by comparing the ^{13}C NMR relaxation times (T1) for host, guest and complexes. The data are given in Tables 1 and 2. Individual carbon assignments were confirmed on the basis of chemical shifts and the 2D HETCOR spectra.

Generally speaking, in liquids, relaxation times (T1) for any given molecule reflect molecular mobility (tumbling) and specific internal motions determined by the internal degrees of freedom of the molecule.[4] The measurement and comparison of T1 values for the same carbon in each complex can give information about the relative stability of the complexes and an intramolecular T1 comparison can lead to estimates of the relative mobilities of the different parts of the macrocyclic ring framework in solution. Compounds with large molecular weights tumble more slowly than smaller molecules and thus exhibit shorter relaxation times than the smaller systems. The formation of a

complex results in an increase in molecular weight, therefore, the complex should tumble more slowly than its components in the free state, resulting in a decrease in T1 values. A T1 comparison between (*S,S*)-(*R*) and (*S,S*)-(*S*) complexes can give information about their relative stabilities, i.e. a consistently larger T1 decrease is seen in the more stable complex. From Table 1, carbons 1-8 show 6.4-51.1% decreases in T1 when the (*S,S*)-(*R*) complex is formed and 1.6-45.8% decreases in T1 when the (*S,S*)-(*S*) complex is formed. From the above arguments we conclude that, the (*S,S*)-(*R*) complex is more stable than the (*S,S*)-(*S*) complex.

It is also sometimes possible to compare T1 values for specific sites within a molecule to understand changes to internal mobility that occur selectively at particular locations, thus giving information about how the complex binds. We had hoped to find greater decreases in T1 for C3, C6, and C7 than for the other periphery carbon atoms upon complexation because they are closer to the proposed tripod hydrogen bonds. The T1 data in Table 1, unfortunately, do not provide conclusive evidence for the specific location of the tripod hydrogen bonds. The T1 data are consistent, however, with the conclusion that hydrogen bonding greatly reduces the flexibility of the macrocycle. As expected, the loss of flexibility increases with increasing distance from the already semi-rigid pyridine ring. Note that in either tripod hydrogen-bonding scheme, the only large scale intramolecular freedom of motion would be concerted rotation about the C-C macrocycle single bonds causing motion of the non-hydrogen-bonded oxygens but not causing motion to any of the macrocycle carbons.

Molecular mechanics conformational searches on (*S,S*)-Me_2P18C6 complexes with

(*R*)- and (*S*)- NapEt in the gas phase yielded the lowest energy conformation, which exhibits $\pi-\pi$ stacking as shown in Figure 2. The (*S*,*S*)-(*R*) complex was 1.734 kcal/mol more stable than (*S*,*S*)-(*S*) complex. The results of molecular mechanics calculations for the rotational energy barriers of the methyl groups in these low energy conformations of the complexes and in the free crown ether are summarized in Table 3. The rotational energy barriers of the methyl groups in both complexes are greater than they are in the free crown ether except Me(A) in the (*S*,*S*)-(*S*) complex, which is still larger than the average for the free ether, predicting a decrease in relaxation times instead of the increase as observed. It is important to note that the data in Table 3 again confirm that the (*S*,*S*)-(*R*) complex is more stable than the (*S*,*S*)-(*S*) complex. There is a much greater energy barrier in the most stable (*S*,*S*)-(*R*) complex indicating a more firmly bound system.

The reasons for the observed increase in T1 for the methyl carbons in both complexes (carbon 9 in Table 1) is not immediately apparent. The increase would normally suggest that the methyl groups have greater mobility in the complex than in the free state. However, as stated in the previous paragraph, the rotational energy barriers of the methyl groups are greater in the complexed form than in the free crown. In liquids, normally extreme narrowing conditions prevail and spin-rotation is the dominant relaxation method so that T1 values correlate with mobility.[5] However, in the case of these methyl groups, a combination of slow tumbling and slow rotation of the methyl groups could cause the dipole-dipole relaxation mechanism to become important. The effect on T1 of the dipole-dipole mechanism is opposite to the normal spin-rotation mechanism and could cause the observed increase in T1.

References

1. R. M. Izatt, C.-Y. Zhu , P. Huszthy, and J. S. Bradshaw, *Enantiomeric Recognition in Macrocycle-Primary Ammonium Cation Systems* in *Crown Ethers: Toward Future Application*; Cooper, S.R., Ed.; VCH Press: New York, in press.
2. D. J. Cram, R, C. Helgeson, L. R. Sousa, J. M. Timko, M. L. A. Domeier, S. C. Peacock K. Maden, and L. Kaplan, *Pure Appl. Chem.* **98**, 107 (1981).
3. R. B. Davidson, N. K. Dalley, R. M. Izatt, J. J. Christensen, J. S. Bradshaw, and C. F. Campana, *Isr. J. Chem.* **25**, 27(1985).
4. Atta-ur Rahman, *Nuclear Magnetic Resonance,* Springer-Verlag, New York, 1986, pp 126-130.
5. F. A. Bovey, *Nuclear Magnetic Resonance Spectroscopy*, 2nd Ed., Academic Press, Inc. San Diego, 1988, p. 261.

Table 1. ^{13}C Relaxation Times (seconds) for (*S*,*S*)-Me_2P18C6 and Its Complexes with (*R*) & (*S*)-NapEt In 1M/1C[a] Mixed Solvent (v/v) at 25°C

Carbon[b]	(*S*,*S*)-Me_2P18C6	(*S*,*S*)-(*R*) Complex[c]		(*S*,*S*)-(*S*) Complex[d]	
	T1	T1	%T1 Decrease	T1	%T1 Decrease
1	1.47	1.29	12.2	1.35	8.2
2	1.26	1.18	6.4	1.24	1.6
3	6.54	4.95	24.3	5.51	15.7
4	1.14	0.88	22.8	0.95	16.7
5	1.81	1.21	33.1	1.26	30.4
6	1.07	0.67	37.4	0.73	31.8
7 & 8	1.31	0.63 & 0.65	51.1	0.71	45.8
9	1.60	1.72	-7.5	1.76	-10.0

[a]M = CD_3OD, C = $CDCl_3$
[b] Numbers correspond to carbons in (*S*,*S*)-$Me_2$18C6 (see structure)
[c](*S*,*S*)-(*R*) = Complex of (*S*,*S*)-Me_2P18C6 with (*R*)-NapEt
[d](*S*,*S*)-(*S*) - Complex of (*S*,*S*)-Me_2P18C6 with (*S*)-NapEt

Table 2. ^{13}C Relaxation Times (seconds) for (*R*) & (*S*) NapEt and Their Complexes with (*S,S*)-Me_2P18C6 in 1M/1C[a] Mixed Solvent (v/v) at 25°C

Carbon[b]	NapEt	(*S,S*)-(*R*) Complex[c]		(*S,S*)-(*S*) Complex[d]	
	T1	T1	%T1 Decrease	T1	%T1 Decrease
A	1.93	1.10	43.0	1.27	34.2
B	2.06	1.21	41.3	1.36	34.0
C	1.75	1.12	36.0	1.23	29.7
D or G	1.75	1.10	26.7	1.23	29.7
E or F	1.81	1.20	33.7	1.28	29.3
F or E	2.14	1.18	44.9	1.41	34.1
G or D	1.78	1.12	37.1	1.25	29.8
H	8.22	4.80	41.6	5.32	35.3
I	7.60	4.45	41.4	5.48	27.9
J	7.70	5.24	31.9	4.65	39.6
K	2.34	1.37	41.4	1.65	29.5
L	1.41	0.90	36.2	0.95	32.6

[a] See footnote a in Table 1
[b] Numbers correspond to carbons in NapEt (see structure)
[c] See footnote c in Table 1
[d] See footnote d in Table 1

Table 3. The Rotational Energy Barriers (Kcal/mol) of Methyl Groups in the Free and Complexed (*S,S*)-Me_2P18C6 From Molecular Mechanics Calculations

	Free Crown Ether		(*S,S*)-(*R*)-Complex		(*S,S*)-(*S*) Complex	
	Me(1)	Me(2)	Me(A)[a]	Me(T)[b]	Me(A)[a]	Me(T)[b]
	3.359	3.444	6.777	9.258	3.409	3.529
Average[c]	3.402			8.018		3.469

[a] Methyl group away from salt
[b] Methyl group toward salt
[c] The average is the only meaningful number as applied to NMR measurements since the molecular mechanics calculations apply to the "lowest" energy conformation. Due to the C_2 symmetry of the ether, and the dynamic equilibria in solution, the methyls are not distinguishable by NMR measurement at room temperature.

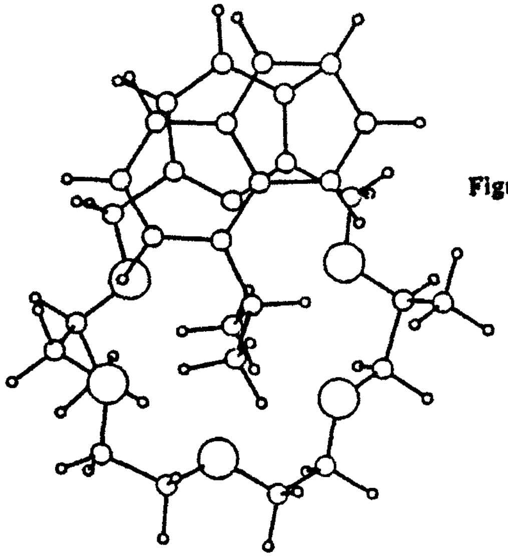


Figure 2a

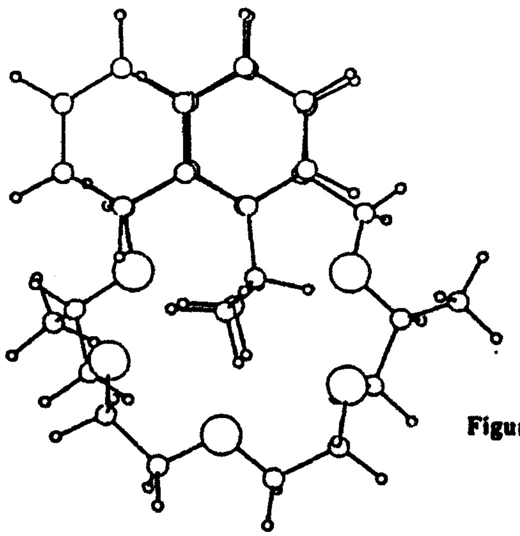
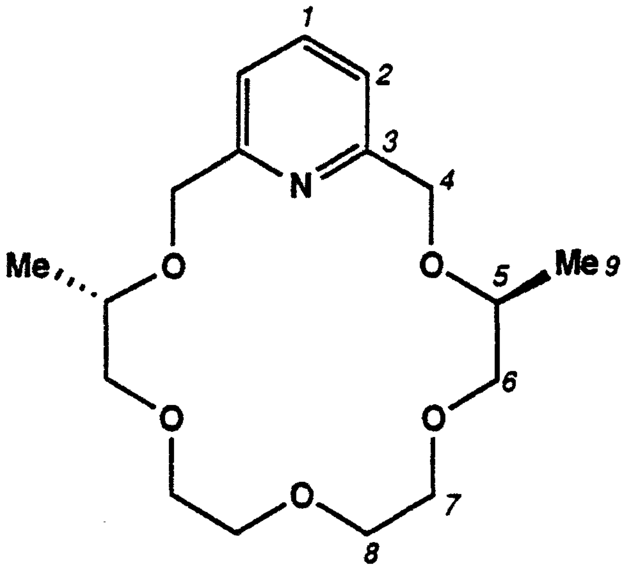


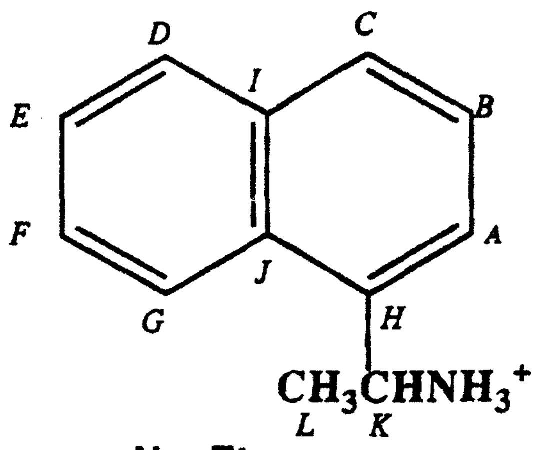
Figure 2b

Figure 2. Computer-generated stereoviews obtained from molecular mechanics calculations of the complexes of the (*S*,*S*)-dimethylpyridino-18-crown-6 with (*R*)-(naphthyl)ethylammonium perchlorate (stereoview a) and with (*S*)-perchlorate (stereoview b)

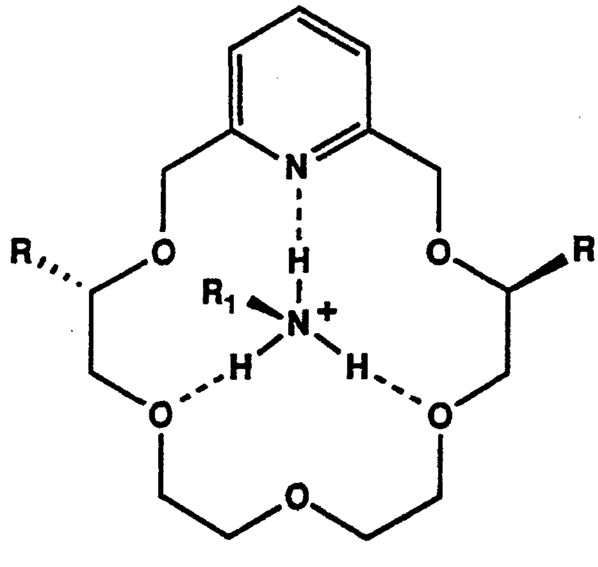
Figure 1. Structures of Compounds



Me_2P18C6



NapEt



Tripod